



## ARTICLE INFO

## Open Access

Received

April 30, 2024

Revised

June 11, 2024

Accepted

July 12, 2024

**\*Corresponding Author**

Khawar Ali Shahzad

E-mail

Khawar.ali@iub.edu.pk

Khawar7bar@yahoo.com

**Keywords**

Peptic ulcer disease

*Helicobacter pylori*

Prevalence

Risk factors

Blood groups

**How to Cite**

Rafiq M, Rizwan M, Ahmad HI, Lashari MH, Shahzad KA. Incidence and risk factors associated with peptic ulcer in different cities of Punjab, Pakistan. Biomedical Letters 2024; 10(1): 51-58.



SCAN ME

# Incidence and risk factors associated with peptic ulcer in different cities of Punjab, Pakistan

Muhammad Rafiq<sup>1</sup>, Muhammad Rizwan<sup>1</sup>, Muhammad Hammad Javed<sup>1</sup>, Hafiz Ishfaq Ahmad<sup>2</sup>, Mushtaq Hussain Lashari<sup>1</sup>, Khawar Ali Shahzad<sup>1\*</sup>

<sup>1</sup>Department of Zoology, The Islamia University of Bahawalpur, Bahawalpur 63100, Pakistan

<sup>2</sup>Department of Animal Breeding and Genetics, The Islamia University of Bahawalpur, Bahawalpur 63100, Pakistan

**Abstract**

Peptic ulcers are severe digestive tract mucosal lesions. Worldwide, peptic ulcer disease (PUD) increases medical costs and morbidity. PUD is rising in Islamabad, Rawalpindi, and Karachi due to lifestyle and changes in diet. PUD is linked to drug and alcohol use, smoking, lack of exercise, and emotional stress. Infection with *Helicobacter pylori*, lack of sleep, and obesity also raise ulcer risk. This study examined the lack of PUD research in three main cities of Punjab (Bahawalpur, Multan, and Lahore). These populations were studied for PUD incidence, complications, risk factors, correlations with other diseases, medications, and blood group linkages. Data was collected by a cross-sectional study from November 2022 to June 2023 on peptic ulcer symptoms in participants aged 11 and above. Questionnaires collected demographic, medical, lifestyle, and nutritional data. Heart rate, blood pressure, and *H. pylori* status were checked. SPSS 25.0 was used to analyze data. Out of 200 participants, 47.5% were men and 52.5% women. There is no correlation between age, gender, or peptic ulcer prevalence in men or women. The sample comprised more rural than urban individuals. Both men and women with peptic ulcers had an O+ blood group. Women had more fever and belly pain. This study shows the prevalence and risk factors of peptic ulcers in urban Pakistan, highlighting the need for prevention and treatment. These findings highlight PUD across genders and suggest future research should consider sample size and self-reporting.



This work is licensed under the Creative Commons Attribution Non-Commercial 4.0 International License.

## Introduction

Peptic ulcers are common gastrointestinal lesions that pose significant health risks worldwide. Peptic Ulcer Disease (PUD), is one of the main causes of hospitalization and mortality globally [1]. Their prevalence has steadily been rising across Pakistan in cities like Islamabad, Rawalpindi, and Karachi due to changes in lifestyle and diet over the last several decades [2, 3].

Alcohol consumption has been linked with peptic ulcers, with heavy drinkers experiencing shorter healing periods and higher incidence rates than moderate drinkers [4]. Smoking compounds this effect, delaying healing timeframes and leading to complications [5]. Dietary factors also play a part; excessive salt intake has been linked with an increased risk of gastric cancer while spicy foods may exacerbate symptoms without actually leading to ulcers [6, 7]. Finally, caffeine, while not directly activating stomach acid production, can worsen ulcers [8].

Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) pose substantial risks; studies have demonstrated their use can damage the upper GI tract, leading to gastroduodenal peptic ulcers and endoscopic lesions [9]. Furthermore, baseline stress has an impact on all forms of ulceration regardless of socioeconomic status, use of NSAIDs, or smoking [10].

*Helicobacter pylori* was first identified in 1982, revolutionizing the understanding and treatment of gastroduodenal diseases by establishing that peptic ulcer disease is an infectious illness requiring antibiotic therapy [11]. *H. pylori* adheres to epithelial cells, releases degradative enzymes and virulence factors into them, and triggers an immune response that damages cells thereby increasing the risk for duodenal and gastric ulcers, gastric Adenocarcinoma and B-cell lymphoma [12].

Regular exercise has been shown to lower the incidence of duodenal ulcers among men. Meanwhile, inactivity and poor sleep can limit melatonin production, an essential hormone needed for bicarbonate secretion and blood flow in the stomach mucosa, thus increasing the risk of *H. pylori* infection [4]. Obesity also puts individuals at an increased risk for gastric ulcers and *H. pylori*-negative ulcers [13].

Blood group O individuals are at higher risk for duodenal ulcers due to an excessive acid output; on the other hand, gastric ulcers that don't involve duodenal ulcers increase gastric cancer risks in blood

group A individuals due to poor acid secretion [14]. A U.S. population study identified older age, obesity, chronic obstructive pulmonary disease (COPD), chronic renal insufficiency (CRI), coronary heart disease, and frequent medical visits as significant risk factors [15].

Historical analyses indicate that gastric and duodenal ulcers were prevalent during the early 20th century; however, their prevalence has steadily decreased due to changes in birth cohorts. The risk was highest for generations born during the 19th century before eventually decreasing over subsequent generations with slight delays for gastric ulcers [16]. By the 20th century, incidence rates had shifted; more men than women experienced gastric ulcers [17].

Peptic ulcer disease remains a potentially life-threatening illness that, left untreated, may lead to life-threatening complications. Signs and symptoms including melena, hematemesis, severe abdominal pain, peritonitis, dysphagia, weight loss, loss of appetite, frequent vomiting episodes, and anemia must all be closely monitored [18, 19].

This study seeks to enhance our understanding of Peptic Ulcer Disease (PUD) in Punjab, Pakistan by providing invaluable insight into preventative measures and targeted interventions across three major cities - Bahawalpur, Multan, and Lahore - with specific objectives such as: Investigating the incidence of PUD in male and female patients, identify complications associated with PUD, analyze risk factors contributing to PUD, examine correlations between PUD and other diseases, assess the impact of permanent medications on PUD and explore associations between blood groups and PUD.

## Materials and Methods

### Study location

The research was carried out across three major cities in Pakistan: Bahawalpur, Multan, and Lahore. Sample collection took place at Bahawal Victoria Hospital (BVH), Nishtar Hospital Multan Al-Sirat Lab Lahore as well as RC Molecular Diagnostic and Research Lab Lahore; patients visiting their gastroenterology units as well as lab visitors participated until 200 samples had been gathered.

### Study population

A cross-sectional study was conducted between November 2022 and June 2023 to investigate the incidence and causes of peptic ulcers. Participants

were required to be 11 years or older, exhibit symptoms of peptic ulcer, and have a history of gastrointestinal surgery, persistent medication use, or previous peptic ulcers. The study considered smoking, alcohol consumption, and NSAID use as factors linked to peptic ulcers. A representative sample was drawn from hospital gastrointestinal wards and laboratories.

### **Ethical considerations**

The study was approved by the institutional review board of each participating institution. Informed consent was obtained from all participants prior to their enrollment in the study.

### **Data collection**

Trained interviewers administered a systematic questionnaire in the local language, which included demographic, medical, lifestyle, and dietary information. Physiological measurements, such as height and weight, were also recorded.

### **Pulse rate calculation**

Participants were instructed to relax and locate their neck or wrist pulse using two fingers, timing the pulse for 60 or 30 seconds, and doubling the count for accuracy. The process was repeated to ensure precision, particularly for irregular heart rhythms.

### **Measurement of blood pressure**

Blood pressure was measured by placing a cuff on the upper arm, gradually inflating it, and using a stethoscope to listen to the heartbeat while releasing pressure. Multiple readings were taken to ensure accuracy.

### **Detection of *H. pylori***

Stool antigen, urea breath, serological, endoscopy with biopsy, and rapid urease tests were utilized to diagnose *H. pylori* infection. This study employed stool antigen and serological tests due to their cost-effectiveness.

### **Detection of *H. pylori* by Serology Test**

To diagnose *H. pylori* using a serology test, the following methodology was applied:

**Blood sampling:** Blood was drawn from the antecubital fossa, hand, or wrist using venipuncture, tourniquet, and sterilization techniques. Samples were packaged and delivered to the lab for testing and stored at the appropriate temperature.

**Serum extraction:** Blood samples were coagulated at 37°C for 10–15 minutes, centrifuged at 1000–2000g for 3-5 minutes to extract serum, and kept in sealed microcentrifuge tubes.

**Detection of *H. pylori* antibodies in serum:** The Healgen immunoassay kit Rapid Test was used to analyze *H. pylori* in serum samples. After adding serum and buffer to the well, test results appeared after 12-15 minutes. Two lines indicated positive *H. pylori* results, while one line indicated negative results. A result with no lines was considered invalid.

### **Detection of *H. pylori* by stool test**

**Sample collection:** Participants were provided with containers and instructions to collect stool samples. They placed a teaspoon of stool in biohazard bags.

**Detection of *H. pylori* antigens in stool:** The Healgen Cassettes Rapid Test was used to analyze *H. pylori* antigens in the stool sample. After buffer dilution for 10 minutes and cassette incubation for 12-15 minutes, results showed two lines (positive), one line (negative), or no lines (invalid).

### **Statistical analysis**

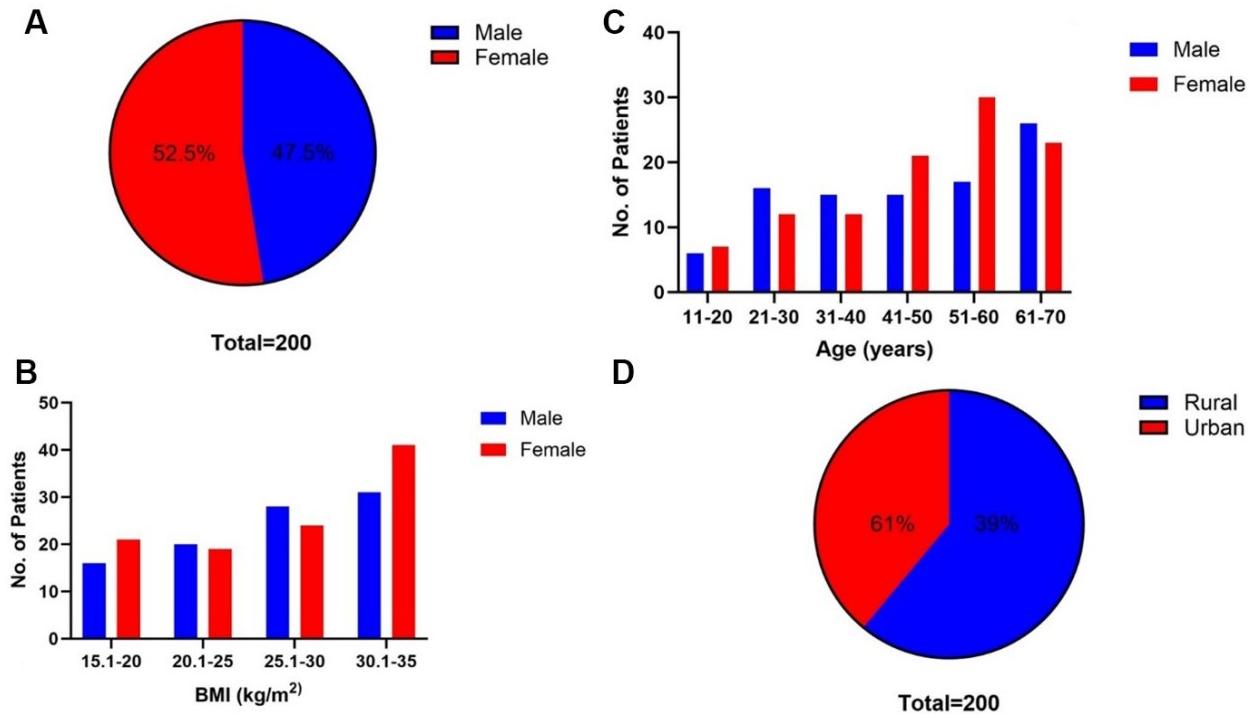
Data analysis was performed using SPSS version 25.0. Descriptive statistics summarized the demographic and clinical characteristics of the study participants. The chi-square test was utilized to compare categorical variables.

## **Results**

This research aimed to determine the prevalence of peptic ulcers in men and women. The study has 200 participants: 95 men (47.5%) and 105 women (52.5%). The population's demographics are shown in **Fig. 1A**. This study examined the age and BMI of peptic ulcer patients, considering gender differences. The 11–20 age group had few participants (3.0% men, 3.5% females). Between 21 and 30, 8.0% were men and 6.0% women. Between 31 and 40, 7.5% were men and 6.0% women. In the 41–50 age range, males were 7.5% and women 10.5%. In the 51–60 age range, 8.5% were men and 15% women. **Fig. 1B** shows 13.0% males and 11.5% females aged 61–70. Neither

gender nor age group had a statistically significant difference in peptic ulcer prevalence (chi-square test,  $p>0.05$ ). As shown in **Fig. 1C**, participants with BMIs of 15.1–20, 20.1–25, 25.1–30, and 30.1–35 were divided. 18.5% of the population had a BMI between 15.1 and 20, 19.5% between 20.1 and 25, 26.0% between 25.1 and 30, and 36.0% between 30.1 and 35. There was no significant variation in peptic ulcer

prevalence by gender or BMI ( $p>0.05$ ). Disease prevalence was compared between rural and urban areas by region. **Fig. 1D** shows that 61% of patients (122 individuals) resided in rural areas and 39% (78 people) in cities. Chi-square tests indicated no correlation ( $p>0.05$ ) between location and peptic ulcer prevalence.

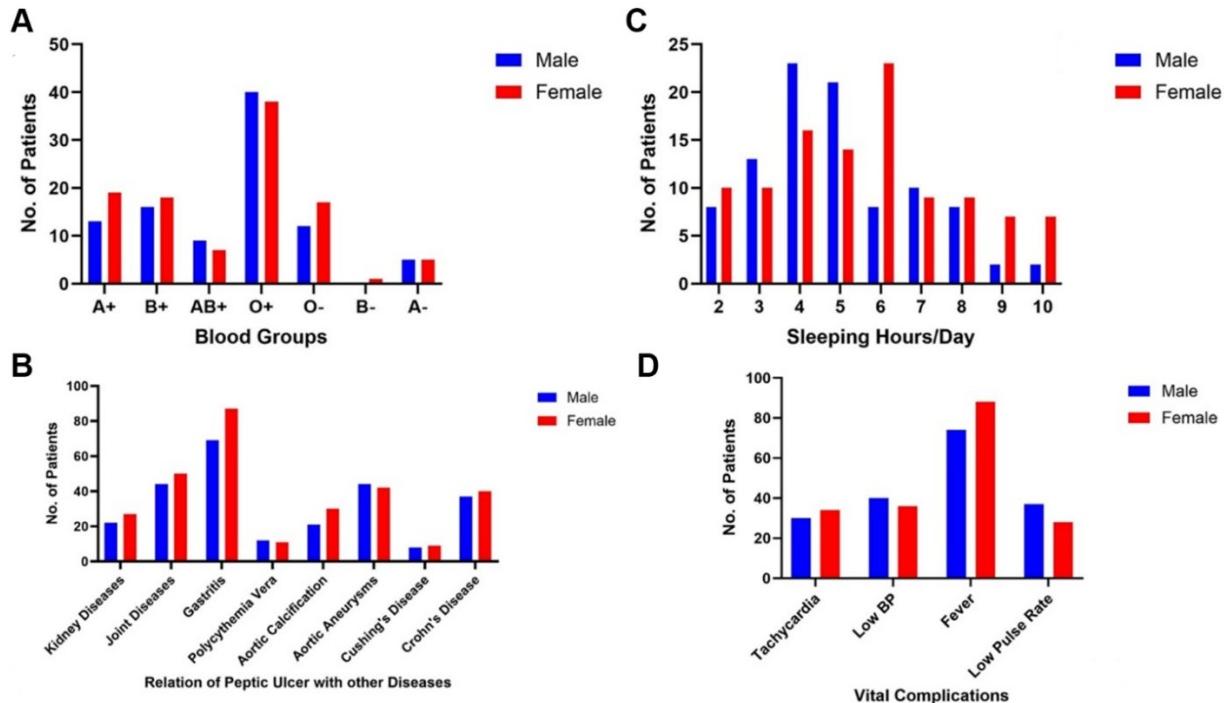


**Fig. 1:** (A) Male to female ratio of peptic ulcer patients (B) Age-wise distribution of peptic ulcer (C) Distribution of peptic ulcer in groups of different BMI (D) Urban and rural population of peptic ulcer patients.

Both men and women with peptic ulcers had blood group analysis. Twenty-six percent of men and 27.5% of women have O blood. **Fig. 2A** shows blood type percentages: O 53.5%, A 21%, B 17.5%, and AB 8%. No statistically significant relationship was established between blood types and peptic ulcer incidence in the patient group. Peptic ulcers and sleep duration were also studied. **Fig. 2B** shows that male patients who slept for 4 hours (11.5%) had the highest incidence, while female patients who slept for 6 hours (11.5%) had the highest rate. The study suggested a relationship between sleep duration and peptic ulcers. Male patients reported 26.5% epigastric discomfort compared to 38.0% female patients. Dyspepsia, heartburn, anemia, melena, chest discomfort, and fatty food intolerance were similar across sexes in **Fig. 2C**. 15.0% of men and 17.0% of women had hypertension or tachycardia, with no statistically significant difference. **Fig. 2D** shows that 18.5% of men and 14.0% of females had low pulse

rates, whereas 37.0% and 44.0% had fever, with a p-value near statistical significance.

17.0% of men and 12.5% of women stated they didn't experience stomach pain, whereas 30.5% and 40% did. Additionally, 25.0% of men and 26.0% of women felt nauseated, whereas 22.5% and 26.5% did not. Only 18.5% of men and 23.0% of women vomited, whereas 29.0% and 29.5% did not. Twenty-five percent of men and 27 percent of women stated they didn't have inadequate urine, whereas 22 percent and 25 percent indicated they did. Men (24.0%) and women (26.0%) were not thirsty, but men (23.5%) and women (26.5%) were. **Fig. 3A** shows no gender differences in symptom prevalence. **Fig. 3B** shows that 6% of men and 11.5% of women ate salty diets. Both men and women ate fast food at 25.0% and 27%, respectively. Female patients drank more tea (46.5%) and coffee (9.5%) than male patients. Sex did not affect consuming highly salty items, fast food, tea, or coffee. **Fig. 3C** shows that 47%



**Fig. 2:** (A) Distribution of peptic ulcer based on blood groups (B) Distribution of peptic ulcer based on sleep (C) Complications due to peptic ulcer (D) Vital complications due to peptic ulcer.

of male and 51.5% of female peptic ulcer patients indicated stress as a cause. Stress intensity varied by gender, but no statistically significant association existed between the two and peptic ulcer etiology. **Fig. 3D** shows that male and female patients had the exact prevalence of *H. pylori* infection (14.5 and 16.5%, respectively). 20.5 percent of men and 30% of women had depression. Neither gender correlated with inherited peptic ulcers.

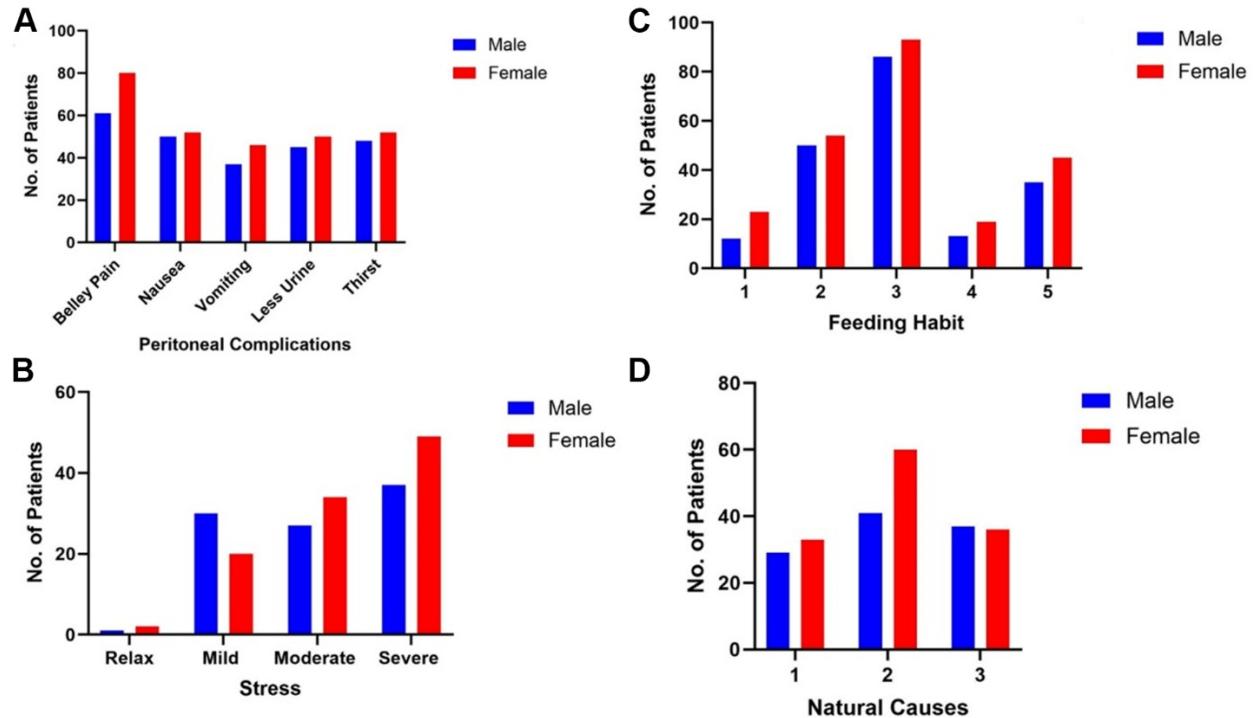
Both male and female peptic ulcer patients had their smoking, drinking, medication, and disease histories examined. 23.5 percent of men smoked, compared to 2.5 percent of women. Smoking correlated with gender ( $\chi^2 = 51.823$ ,  $p = 0.001^*$ ). Only 3% of patients drink. Also, gender did not significantly affect alcohol consumption ( $p = 0.074$ ). Figure 4 (A) shows the smoker-alcoholic peptic ulcer ratio. 14.5% of men and 21.0% of women use corticosteroids. **Fig. 4B** shows that 22.1% of male and 26.5% of female patients used NSAIDs. Corticosteroid and NSAID usage were not significantly different across the sexes ( $p = 0.162$  and 0.701, respectively).

Renal illness affects 11.0 percent of male peptic ulcer patients and 13.5 percent of females. Renal disease was common in peptic ulcer patients ( $p = 0.675$ ). Sexes had comparable rates of joint disease (25.5 percent male and 22.0 percent female;  $p = 0.854$ ). 13 percent of men and 34.5 percent of women had gastritis. The

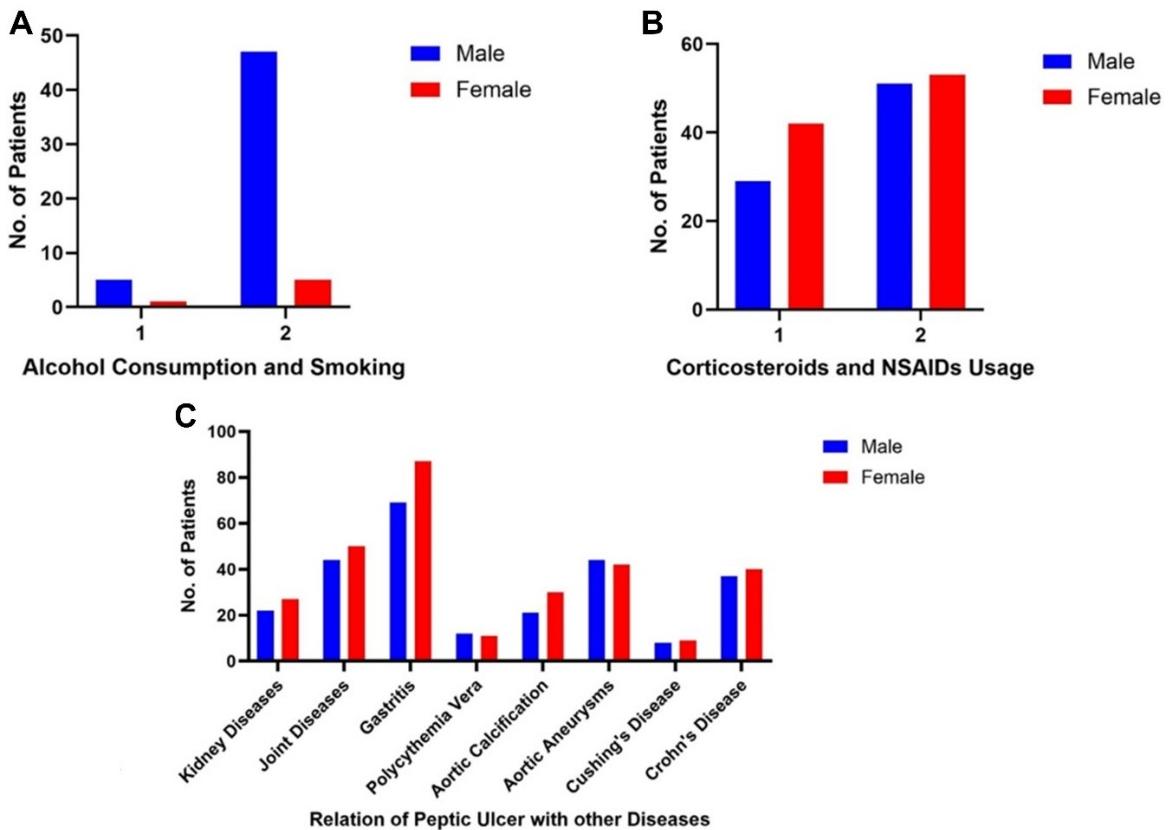
distinction was not significant ( $p = 0.081$ ). Polycythemia vera was equally prevalent in men and women (6.0% and 5.5%, respectively;  $p = 0.633$ ). Aortic calcification was 35.5% in women and 10.5% in males. Aortic aneurysms affected 22% of men and 21% of women. Peptic ulcer patients had identical rates of Cushing's and Crohn's diseases ( $p = 0.970$  and 0.902, respectively). The proportion of male and female patients with various illnesses is given in **Fig. 4C**. The investigation found no significant differences in peptic ulcer disease incidence between men and women.

## Discussion

This study included 200 patients, comprising 47.5% males and 52.5% females. Previous research has shown that females have a higher rate of PUD compared to males [20]. Climate, nutrition, and lifestyle factors all play a role in the prevalence of peptic ulcers for both genders [21, 22]. Peptic ulcers were most frequently seen among individuals aged 51-60 with prevalence increasing until age 60 and then decreasing after that. A Japanese study also discovered peptic ulcers to be more prevalent among middle-aged and older individuals [23] while higher BMI categories may increase the incidence [24]. Additionally, 61% of cases originated in rural locations while 39% were in urban areas -



**Fig. 3:** (A) Peritoneal complications due to peptic ulcer disease (B) Feeding habits of peptic ulcer disease (C) Stress levels in peptic ulcer patients (D) Natural causes of peptic ulcer.



**Fig. 4:** (A) Smoking and alcohol consumption in peptic ulcer patients (B) Corticosteroids and NSAIDs usage (C) Relation of peptic ulcer with other diseases.

reflecting similar trends seen among rural China and Egypt [25]. Studies have linked A+ and B+ blood groups with peptic ulcers; however, blood type O+ was found to be most prevalent (both male and female patients [14, 26] Furthermore, Peptic Ulcer prevalence was linked with shorter sleep durations: specifically between 4-5 and 6 hours for males and 6 hours and more for females - supporting recent research which indicates regular restful sleep is essential for optimal gut health [27, 28]. This research explored various symptoms associated with peptic ulcer diseases, such as epigastric discomfort, dyspepsia, nausea, anemia, melena chest pain, and sensitivity to fatty foods [29]. Men and female patients demonstrated distinct variations in both appearance and severity of symptoms, with female patients showing more signs of tachycardia, low blood pressure, and pulse rates than their male counterparts [30, 31]. Women experienced higher fevers while both genders reported comparable stomach pain, nausea, and vomiting [32]. Previous research demonstrated that 47.5% of patients experienced decreased urine flow while both genders reported thirst [33]. Multiple patients reported eating high-salt food items, fast food, tea, coffee, and spicy dishes - consistent with findings from Istanbul research [4]. Furthermore, factors like stress, alcohol consumption, and smoking were identified as possible contributors to their peptic ulcer condition.

This study investigated the correlations among corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), depression, family history, and *H. pylori* infection on risk for peptic ulcers. Studies have repeatedly linked *H. pylori* with peptic ulcer disease [34, 35], while prior research indicates a strong association between depression and peptic ulcer disease. Studies also highlight depression's strong link with peptic ulcer disease, underscoring its significance during gastro-intestine illness cases [36, 37]. Furthermore, family histories of peptic ulcers increase one's likelihood of contracting the condition [38], while corticosteroids and NSAIDs may increase its risk; which corresponds with the existing literature [39]. This research explores trends of peptic ulcers in Pakistan and their increasing prevalence, while simultaneously showing their prevention and treatment measures are necessary and urgent; yet due to self-reported data and limited sample sizes more comprehensive research should be conducted.

## Conclusion

This research conducted a detailed examination of males and females across different socioeconomic

statuses to compare rates of peptic ulcer prevalence between them, finding no differences in age groups, gender, or blood types; daily sleep duration may influence prevalence, with female patients reporting increased pain after eating or at midnight; no gender variations in symptoms were identified. The consequences of peptic ulcers were similar in men and women. Women consumed more tea and coffee than men, but their intake of salty and fast food was similar. Gender did not significantly affect stress levels but was substantially associated with depression, though not with *H. pylori* infection. Additionally, certain illnesses had modest relationships with peptic ulcers. These findings provide valuable insights for medical professionals and investigators in understanding the frequency and risk factors of peptic ulcers in both sexes.

## Acknowledgment

We extend our deepest gratitude to all the participants who took part in this study, without whom this research would not have been possible. Special thanks are due to the staff at Bahawal Victoria Hospital, Nishtar Hospital Multan, Al-Sirat Lab Lahore, and RC Molecular Diagnostic and Research Lab Lahore for their support in data collection.

## Conflict of interest

The authors declare no conflict of interest.

## References

- [1] Kavitt RT, Lipowska AM, Anyane-Yeboa A, Gralnek IM. Diagnosis and treatment of peptic ulcer disease. *The American journal of medicine*. 2019;132:447-56.
- [2] Reitsma MB, Kendrick PJ, Ababneh E, Abbafati C, Abbasi-Kangevari M, Abdoli A, et al. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. *The Lancet*. 2021;397:2337-60.
- [3] Rashid MN, Soomro AM, Channa NA, Laghari ZA. Prevalence of different types of peptic ulcer disease and treatment modalities used by patients in Hyderabad, Sindh. *Pakistan Journal of Physiology*. 2016;12:6-9.
- [4] Yegen BC. Lifestyle and peptic ulcer disease. *Current pharmaceutical design*. 2018;24:2034-40.
- [5] Li L, Chan R, Lu L, Shen J, Zhang L, Wu W, et al. Cigarette smoking and gastrointestinal diseases: the causal relationship and underlying molecular mechanisms. *International journal of molecular medicine*. 2014;34:372-80.
- [6] Raei N, Behrouz B, Zahri S, Latifi-Navid S. *Helicobacter pylori* infection and dietary factors act synergistically to

- promote gastric cancer. *Asian Pacific Journal of Cancer Prevention.* 2016;17:917-21.
- [7] Singh A, VL AB, Azamthulla M. Herbal Remedies Used for the Treatment of Peptic Ulcer.
- [8] Khesbak AA. Study of Some Affecting Factors on the Infection with Peptic Ulcer. *Ind J Pure App Biosci.* 2023;11:42-9.
- [9] Melcarne L, García-Iglesias P, Calvet X. Management of NSAID-associated peptic ulcer disease. *Expert Review of Gastroenterology & Hepatology.* 2016;10:723-33.
- [10] Levenstein S, Rosenstock S, Jacobsen RK, Jorgensen T. Psychological stress increases risk for peptic ulcer, regardless of *Helicobacter pylori* infection or use of nonsteroidal anti-inflammatory drugs. *Clinical Gastroenterology and Hepatology.* 2015;13:498-506. e1.
- [11] Mégraud F, Lehours P. *Helicobacter pylori* detection and antimicrobial susceptibility testing. *Clinical microbiology reviews.* 2007;20:280-322.
- [12] Ahmed S, Belayneh YM. *Helicobacter pylori* and duodenal ulcer: systematic review of controversies in causation. *Clinical and Experimental Gastroenterology.* 2019;441-7.
- [13] Boylan MR, Khalili H, Huang ES, Chan AT. Measures of adiposity are associated with increased risk of peptic ulcer. *Clinical Gastroenterology and Hepatology.* 2014;12:1688-94.
- [14] Abdulridha MK. The relationship between ABO blood group distribution and the incidence of upper gastric and duodenal ulcer in Iraqi patients. *Iraqi Journal of Pharmaceutical Sciences (P-ISSN 1683-3597 E-ISSN 2521-3512).* 2013;22:97-103.
- [15] Garro D, Delegge MH. Risk factors for gastrointestinal ulcer disease in the US population. *Digestive Diseases and Sciences.* 2010;55:66-72.
- [16] Sonnenberg A. Birth cohort patterns of gastric cancer and peptic ulcer among non-whites in the USA. *J Epidemiol Community Health.* 2011;65:1059-64.
- [17] Sonnenberg A. historic changes of *Helicobacter pylori*-associated diseases. *Alimentary pharmacology & therapeutics.* 2013;38:329-42.
- [18] Malik TF, Gnanapandithan K, Singh K. Peptic ulcer disease. 2018.
- [19] Sverdén E, Agréus L, Dunn JM, Lagergren J. Peptic ulcer disease. *Bmj.* 2019;367.
- [20] Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. *BMC gastroenterology.* 2022;22:58.
- [21] Suzuki RB, Cola RF, Cola LTB, Ferrari CG, Ellinger F, Therezo AL, et al. Different risk factors influence peptic ulcer disease development in a Brazilian population. *World Journal of Gastroenterology: WJG.* 2012;18:5404.
- [22] Chalya PL, Mabula JB, Koy M, Mcchembe MD, Jaka HM, Kabangila R, et al. Clinical profile and outcome of surgical treatment of perforated peptic ulcers in Northwestern Tanzania: A tertiary hospital experience. *World Journal of Emergency Surgery.* 2011;6:1-10.
- [23] Bae S, Shim K-N, Kim N, Kang JM, Kim D-S, Kim K-M, et al. Incidence and short-term mortality from perforated peptic ulcer in Korea: a population-based study. *Journal of epidemiology.* 2012;22:508-16.
- [24] Pyo JH, Lee H, Kim JE, Choi YH, Kim TJ, Min YW, et al. Obesity and risk of peptic ulcer disease: a large-scale health check-up cohort study. *Nutrients.* 2019;11:1288.
- [25] Shamseya AM, Shamseya MM, Salem MA, Ahmed AS, Abdelfatah DA. Assessment of some health-related practices and knowledge among a group of Egyptian patients with peptic ulcer disease. *J Med Sci Clin Res.* 2015;3:8186-92.
- [26] Edgren G, Hjalgrim H, Rostgaard K, Norda R, Wikman A, Melbye M, et al. Risk of gastric cancer and peptic ulcers in relation to ABO blood type: a cohort study. *American journal of epidemiology.* 2010;172:1280-5.
- [27] Shiao T-H, Liu C-J, Luo J-C, Su K-C, Chen Y-M, Chen T-J, et al. Sleep apnea and risk of peptic ulcer bleeding: a nationwide population-based study. *The American journal of medicine.* 2013;126:249-55. e1.
- [28] Fang B, Yang S, Xu R, Chen G. Association between poor sleep quality and subsequent peptic ulcer recurrence in older patients with mild cognitive impairment: Examining the role of social engagement. *Scientific Reports.* 2019;9:2188.
- [29] Dunlap JJ, Patterson S. Peptic ulcer disease. *Gastroenterology Nursing.* 2019;42:451-4.
- [30] Jung SH, Oh JH, Lee HY, Jeong JW, Go SE, You CR, et al. Is the AIMS65 score useful in predicting outcomes in peptic ulcer bleeding? *World journal of gastroenterology: WJG.* 2014;20:1846.
- [31] Chung KT, Shelat VG. Perforated peptic ulcer-an update. *World journal of gastrointestinal surgery.* 2017;9:1.
- [32] ANDERSON III WD, Strayer SM. Evaluation of nausea and vomiting in adults: a case-based approach. *American Family Physician.* 2013;88:371-9.
- [33] Tarasconi A, Coccolini F, Biffl WL, Tomasoni M, Ansaldi L, Picetti E, et al. Perforated and bleeding peptic ulcer: WSES guidelines. *World journal of emergency surgery.* 2020;15:1-24.
- [34] Tsukanov VV, Kasparov EV, Tonkikh JL, Shtygasheva OV, Butorin NN, Amelchugova OS, et al. Peptic ulcer disease and *Helicobacter pylori* infection in different Siberian ethnicities. *Helicobacter.* 2017;22:e12322.
- [35] Chang W-L, Yeh Y-C, Sheu B-S. The impacts of *H. pylori* virulence factors on the development of gastroduodenal diseases. *Journal of biomedical science.* 2018;25:1-9.
- [36] Kim SY, Min C, Oh DJ, Choi HG. Reciprocal association between depression and peptic ulcers: Two longitudinal follow-up studies using a national sample cohort. *Scientific Reports.* 2020;10:1749.
- [37] Wu Y, Murray GK, Byrne EM, Sidorenko J, Visscher PM, Wray NR. GWAS of peptic ulcer disease implicates *Helicobacter pylori* infection, other gastrointestinal disorders and depression. *Nature communications.* 2021;12:1146.
- [38] Mhaskar RS, Ricardo I, Azliyati A, Laxminarayan R, Amol B, Santosh W, et al. Assessment of risk factors of *Helicobacter pylori* infection and peptic ulcer disease. *Journal of global infectious diseases.* 2013;5:60.
- [39] Tomizawa M, Shinozaki F, Hasegawa R, Shirai Y, Motoyoshi Y, Sugiyama T, et al. Immunosuppressive agents are associated with peptic ulcer bleeding. *Experimental and Therapeutic Medicine.* 2017;13:1927-31.